

Claims:

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1. A method of diagnosing osteoporosis or predisposition to osteoporosis in an individual comprising determining the genotype of an intron in a TGF- $\beta$  gene.
  2. A method according to Claim 1 wherein said intron is intron 5 of a TGF- $\beta$  gene.
  3. A method according to Claim 2 wherein presence of a *Bst*UI restriction site in said intron 5 is correlated with increased risk of osteoporosis or predisposition to osteoporosis.
  4. A method according to any previous claim wherein said TGF- $\beta$  gene is the TGF- $\beta$ 1 gene.
  5. A method according to the previous claim comprising amplifying a portion of said individual's TGF- $\beta$  gene, said portion including at least one intron, by using PCR techniques.
  6. An isolated DNA molecule comprising the sequence of SEQ ID NO: 1.
  7. A kit for diagnosis of osteoporosis or predisposition to osteoporosis comprising PCR primers for use in amplification of an intron in a TGF- $\beta$  gene, and reference means to enable determination of the genotype of said intron.
  8. A kit according to Claim 7 wherein said intron is intron 5 of a TGF- $\beta$  gene.
  9. A kit according to Claim 7 or 8 wherein said TGF- $\beta$  gene is a TGF- $\beta$ 1 gene.
  10. A kit according to any of Claims 7-9 wherein said PCR primers comprise SEQ ID NO: 2.

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11. A kit according to any of Claims 7-10 wherein said PCR primers comprise SEQ ID NO:3.
  12. A kit according to any of Claims 7-10 further comprising the restriction enzyme *Bst*UI.
  13. A method of osteoporosis therapy comprising:-  
  
screening an individual for a genetic predisposition to osteoporosis; and  
  
if such a predisposition is identified, treating that individual to prevent osteoporosis or to delay onset of osteoporosis, wherein a predisposition to osteoporosis is correlated with a polymorphism in an intron of a TGF- $\beta$ 1 gene.
  14. A method according to Claim 12 wherein said polymorphism is in intron 5 of the TGF- $\beta$ 1 gene.
  15. A method according to Claim 14 in which a predisposition to osteoporosis is correlated with the presence of a *Bst*UI restriction site in intron 5 of a TGF- $\beta$ 1 gene.
  16. A method according to any of Claims 13-15 in which a predisposition to osteoporosis is correlated with a substitution of a thymidine with a cytosine at position 31 in SEQ ID NO:1.
  17. A method of treating an individual predisposed or susceptible to osteoporosis said method comprising:-
    - (a) determining the genotype of an intron in a TGF- $\beta$ 1 gene in said individual in order to identify a risk genotype in said TGF- $\beta$ 1 gene; and

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(b) administering to said individual an effective dose of a therapeutic composition suitable to delay, reduce, or prevent osteoporosis in said animal.

18. The method of Claim 17 comprising administering to said individual an effective dose of said therapeutic composition selected from a group consisting of steroid hormones, isoflavones, calcium supplements, bisphosphonates, calcitonin, sodium fluoride, parathyroid hormone and calcitriol.
19. A method for predicting response to osteoporosis therapy, comprising diagnosing genotype of an intron in a TGF- $\beta$  gene according to the method of claim 1.
20. Use, in the manufacture of means for assessing whether an individual has a predisposition to osteoporosis, of PCR primers adapted to amplify a region of a TGF- $\beta$  gene, said region including intron 5.
21. Use according to Claim 20 wherein said TGF- $\beta$  gene is a TGF- $\beta$ 1 gene.
22. A method of determining bone mineral density in an individual comprising determining the genotype of an intron in a TGF- $\beta$  gene.
23. A method of determining risk of fracture in an individual comprising determining the genotype of an intron in an TGF- $\beta$  gene.
24. A method of determining bone turnover in an individual comprising determining the genotype of an intron in a TGF- $\beta$  gene.
25. A method according to any of claims 22-24 wherein said intron is intron 5 of a TGF- $\beta$ 1 gene.

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26. A method according to Claim 25 wherein identification of a *Bst*UI restriction site in said intron 5 is diagnostic of increased risk and absence of said *Bst*UI restriction site is diagnostic of reduced risk.
27. A method of diagnosing osteoarthritis and predisposition to osteoarthritis in an individual comprising determining the genotype of intron 5 in a TGF- $\beta$ 1 gene.

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